

10/764,676  
10/479,080

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|--------------|-----------|--|
| NEWS         | 1         | Web Page URLs for STN Seminar Schedule - N. America  |
| NEWS         | 2         | "Ask CAS" for self-help around the clock   |
| NEWS         | 3 SEP 01  | New pricing for the Save Answers for SciFinder Wizard within STN Express with Discover!  |
| NEWS         | 4 OCT 28  | KOREPAT now available on STN   |
| NEWS         | 5 NOV 30  | PHAR reloaded with additional data   |
| NEWS         | 6 DEC 01  | LISA now available on STN  |
| NEWS         | 7 DEC 09  | 12 databases to be removed from STN on December 31, 2004   |
| NEWS         | 8 DEC 15  | MEDLINE update schedule for December 2004  |
| NEWS         | 9 DEC 17  | ELCOM reloaded; updating to resume; current-awareness alerts (SDIs) affected   |
| NEWS         | 10 DEC 17 | COMPUAB reloaded; updating to resume; current-awareness alerts (SDIs) affected   |
| NEWS         | 11 DEC 17 | SOLIDSTATE reloaded; updating to resume; current-awareness alerts (SDIs) affected  |
| NEWS         | 12 DEC 17 | CERAB reloaded; updating to resume; current-awareness alerts (SDIs) affected   |
| NEWS         | 13 DEC 17 | THREE NEW FIELDS ADDED TO IFIPAT/IFIUDB/IFICDB   |
| NEWS         | 14 DEC 30 | EPFULL: New patent full text database to be available on STN   |
| NEWS         | 15 DEC 30 | CAPLUS - PATENT COVERAGE EXPANDED  |
| NEWS         | 16 JAN 03 | No connect-hour charges in EPFULL during January and February 2005   |
| NEWS         | 17 FEB 25 | CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered   |
| NEWS         | 18 FEB 10 | STN Patent Forums to be held in March 2005   |
| NEWS         | 19 FEB 16 | STN User Update to be held in conjunction with the 229th ACS National Meeting on March 13, 2005  |
| NEWS         | 20 FEB 28 | PATDPAFULL - New display fields provide for legal status data from INPADOC   |
| NEWS         | 21 FEB 28 | BABS - Current-awareness alerts (SDIs) available   |
| NEWS         | 22 FEB 28 | MEDLINE/LMEDLINE reloaded  |
| NEWS         | 23 MAR 02 | GBFULL: New full-text patent database on STN   |
| NEWS         | 24 MAR 03 | REGISTRY/ZREGISTRY - Sequence annotations enhanced   |
| NEWS         | 25 MAR 03 | MEDLINE file segment of TOXCENTER reloaded   |
| NEWS         | 26 MAR 22 | KOREPAT now updated monthly; patent information enhanced   |
| NEWS         | 27 MAR 22 | Original IDE display format returns to REGISTRY/ZREGISTRY  |
| NEWS         | 28 MAR 22 | PATDPASPC - New patent database available  |
| NEWS         | 29 MAR 22 | REGISTRY/ZREGISTRY enhanced with experimental property tags  |
| NEWS EXPRESS |           | JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005 |

10/479,080

|            |   |
|------------|---|
| NEWS HOURS | STN Operating Hours Plus Help Desk Availability         |
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| NEWS LOGIN | Welcome Banner and News Items                           |
| NEWS PHONE | Direct Dial and Telecommunication Network Access to STN |
| NEWS WWW   | CAS World Wide Web Site (general information)           |

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FILE 'REGISTRY' ENTERED AT 20:19:40 ON 23 MAR 2005  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 22 MAR 2005 HIGHEST RN 847018-75-1  
DICTIONARY FILE UPDATES: 22 MAR 2005 HIGHEST RN 847018-75-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

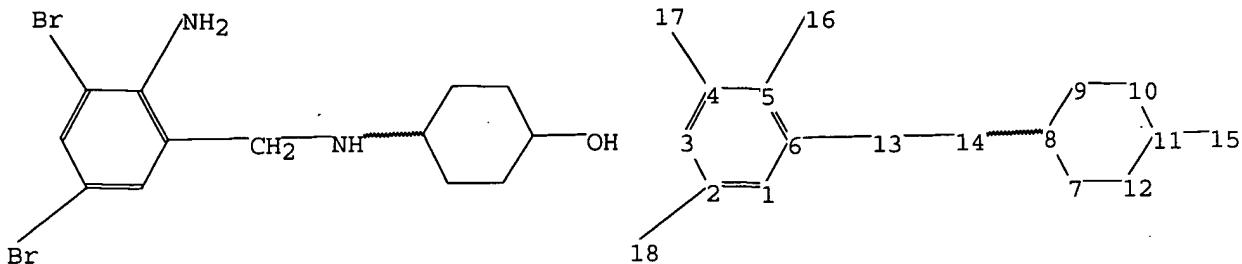
\*\*\*\*\*  
\*  
\* The CA roles and document type information have been removed from \*  
\* the IDE default display format and the ED field has been added, \*  
\* effective March 20, 2005. A new display format, IDERL, is now \*  
\* available and contains the CA role and document type information. \*  
\*  
\*\*\*\*\*

Crossover limits have been increased. See **HELP CROSSOVER** for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> Uploading C:\Program Files\Stnexp\Queries\10479080.str

~~107479,080~~ 10(764,676



chain nodes :

13 14 15 16 17 18

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12

chain bonds :

2-18 4-17 5-16 6-13 8-14 11-15 13-14

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12

exact/norm bonds :

5-16 8-14 11-15

exact bonds :

2-18 4-17 6-13 7-8 7-12 8-9 9-10 10-11 11-12 13-14

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 : 7 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS

L1 STRUCTURE UPLOADED

=> s 11 ful  
FULL SEARCH INITIATED 20:20:10 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 142 TO ITERATE

100.0% PROCESSED 142 ITERATIONS  
SEARCH TIME: 00.00.01

39 ANSWERS

L2 39 SEA SSS FUL L1

| => file caplus      | COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|---------------------|----------------------|------------------|---------------|
| FULL ESTIMATED COST |                      | 161.33           | 161.54        |

FILE 'CAPLUS' ENTERED AT 20:20:17 ON 23 MAR 2005  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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FILE COVERS 1907 - 23 Mar 2005 VOL 142 ISS 13  
FILE LAST UPDATED: 22 Mar 2005 (20050322/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 12  
L3 501 L2

=> s 13 and (lipid or lipoic acid)  
249520 LIPID  
201149 LIPIDS  
311320 LIPID  
(LIPID OR LIPIDS)  
3317 LIPOIC  
3953527 ACID  
1469296 ACIDS  
4429774 ACID  
(ACID OR ACIDS)  
3275 LIPOIC ACID  
(LIPOIC(W)ACID)  
L4 24 L3 AND (LIPID OR LIPOIC ACID)

=> d 14 ibib hitstr abs 1-24

L4 ANSWER 1 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2004:965034 CAPLUS  
DOCUMENT NUMBER: 141:400958  
TITLE: Drug formulations with methacrylic acid-methylacrylate-ethylacrylate-butylmethacrylate copolymer containing coating or matrix  
INVENTOR(S): Petereit, Hans-Ulrich; Meier, Christian; Schultes, Klaus  
PATENT ASSIGNEE(S): Roehm G.m.b.H. & Co. K.-G., Germany  
SOURCE: PCT Int. Appl., 47 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|--|------|----------|-----------------|----------|
| WO 2004096185  | A1   | 20041111 | WO 2004-EP2061  | 20040302 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, |      |          |                 |          |

NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,  
 TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,  
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,  
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,  
 SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,  
 TD, TG  
 DE 10319458 A1 20041118 DE 2003-10319458 20030429  
 EP 1496870 A1 20050119 EP 2004-716230 20040302  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK  
 PRIORITY APPLN. INFO.: DE 2003-10319458 A 20030429  
 WO 2004-EP2061 W 20040302

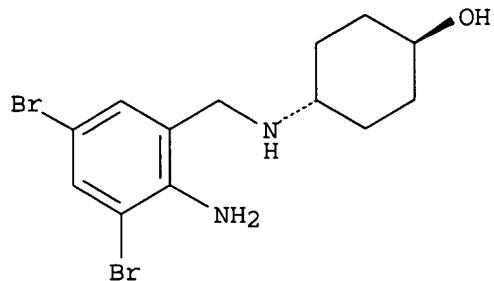
IT 18683-91-5, Ambroxol

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (drug formulations with methacrylic acid-methylacrylate-ethylacrylate-  
 butylmethacrylate copolymer containing coating or matrix)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



AB The invention relates to a method for producing a coated dosage form or a dosage form in the form of a matrix containing an active substance. The dosage form is produced by processing a copolymer that contains a pharmaceutical active substance, an optional core and/or pharmaceutically conventional aggregates in a manner known per se by melting, injection-molding, extrusion, wet granulation, casting, dipping, spreading, spraying or compaction to give a coated dosage form and/or to give a matrix containing an active substance. The method is characterized in that a copolymer is used that is composed of 20 to 33 % by weight of methacrylic acid, 5 to 30 % by weight of Me acrylate, 20 to 40 % by weight of

Et acrylate, and more than 10 to 30 % by weight of Bu methacrylate and optionally 0 to 10 % by weight of addnl. vinylically copolymerizable monomers, with the proviso that the glass temperature of the copolymer is 55 to 70° according to ISO 11357-2, item 3.3.3. The invention also relates to the dosage form produced according to the invention, to the copolymer and to the use thereof. Thus a copolymer composed of (weight/weight%): methacrylic acid 30; methylacrylate 20; ethylacrylate 30 and butylmethacrylate 20 was used for the coating of quinidine sulfate; 469.7 g of the emulsion copolymerizate was mixed with 8.5 g polysorbate 80 (33% aqueous solution), 7.0 g glycerol monostearate and 268.7 g water. The coating suspension was applied in a spray-coating apparatus onto 200 g quinidine sulfate cores to result a 6.0 mg/cm<sup>2</sup> coating.

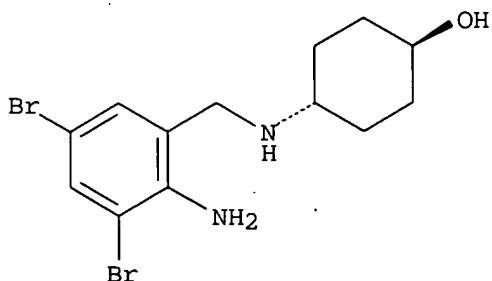
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:625142 CAPLUS  
 DOCUMENT NUMBER: 141:134112  
 TITLE: Drug combination comprising alpha-lipoic acid, ambroxol and/or inhibitors of the angiotensin converting enzyme (ACE) for use in the prevention and treatment of neurodegenerative diseases  
 INVENTOR(S): Ansorge, Siegfried; Roehnert, Peter; Striggow, Frank; Taeger, Michael; Reymann, Klaus; Schroeder, Ulrich  
 PATENT ASSIGNEE(S): Keyneurotek A.-G., Germany; IMTM G.m.b.H.  
 SOURCE: Eur. Pat. Appl., 20 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.   | KIND | DATE     | APPLICATION NO.  | DATE       |
|--|------|----------|------------------|------------|
| EP 1442743   | A1   | 20040804 | EP 2004-1224     | 20040121   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  |      |          |                  |            |
| DE 10303229  | A1   | 20040826 | DE 2003-10303229 | 20030128   |
| CA 2455246   | AA   | 20040728 | CA 2004-2455246  | 20040116   |
| US 2004219207  | A1   | 20041104 | US 2004-764676   | 20040126   |
| JP 2004307467  | A2   | 20041104 | JP 2004-18916    | 20040127   |
| PRIORITY APPLN. INFO.: IT 18683-91-5, Ambroxol   |      |          | DE 2003-10303229 | A 20030128 |
| RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  |      |          |                  |            |
| (drug combination comprising alpha-lipoic acid, ambroxol and/or inhibitors of angiotensin converting enzyme (ACE) for use in prevention and treatment of neurodegenerative diseases) |      |          |                  |            |
| RN 18683-91-5 CAPLUS   |      |          |                  |            |
| CN Cyclohexanol, 4-[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)  |      |          |                  |            |

Relative stereochemistry.

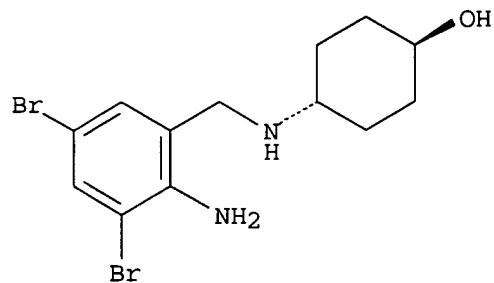


AB The invention concerns a drug combination comprising alpha-lipoic acid, ambroxol and/or inhibitors of the angiotensin converting enzyme (ACE), e.g. enalapril, for use in the prevention and treatment of neurodegenerative diseases. The activity of the combination is based on the fact that damaged neuronal cells exhibit fewer thiol groups than other CNS cells and that the drug combination is able to diminish the damage by

40-45 %. A typical combination that was used for tissue culture expts. included 10  $\mu$ g/mL  $\alpha$ - **lipoic acid**, 10  $\mu$ M ambroxol and 20  $\mu$ g/mL enalapril.

L4 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2004:443865 CAPLUS  
 DOCUMENT NUMBER: 141:186294  
 TITLE: Effect of paraquat intoxication and ambroxol treatment on hydrogen peroxide production and **lipid** peroxidation in selected organs of rat  
 AUTHOR(S): Anguelov, Anguel; Chichovska, Maria  
 CORPORATE SOURCE: Regional Veterinary Station, Plovdiv, Bulg.  
 SOURCE: Veterinarski Arhiv (2004), 74(2), 141-155  
 CODEN: VEARA6; ISSN: 0372-5480  
 PUBLISHER: University of Zagreb, Faculty of Veterinary Medicine  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 18683-91-5, Ambroxol  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
 (paraquat intoxication and ambroxol treatment effect on hydrogen peroxide production and **lipid** peroxidn. in selected organs of rat)  
 RN 18683-91-5 CAPLUS  
 CN Cyclohexanol, 4-[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



AB Expts. with the herbicide paraquat were carried out on Wistar rats. The concentration of hydrogen peroxide ( $H_2O_2$ ) and various **lipid** peroxidn. products (LPP), such as conjugated dienes (CD), **lipid** peroxides (LH), malonyl-dialdehyde (MDA) and Schiff bases in selected organs of the rat given a single intra-peritoneal dose of 35 mg/kg-1 paraquat was examined. The influence of a mucolytic and probably antioxidant drug, ambroxol, on paraquat-induced changes in the concentration of  $H_2O_2$  and LPP was also examined. Paraquat increased the pulmonic, cardiac and hepatic concentration of  $H_2O_2$ , CD, LH and MDA approx. fourfold. Although the dose of paraquat was nearly twice the LD50 dose, it did not noticeably increase the concentration of these substances in the kidney. Ambroxol alleviated the increase of  $H_2O_2$  in the liver but did not reduce the concentration of CD, LH and CD. The results indicate that ambroxol did not alleviate the increase the pulmonic concentration of  $H_2O_2$ , but protected the increase in the concentration of CD and MDA. Moreover, the drug administration alone induced **lipid** peroxidn. in the liver. Ambroxol alone acts as a pro-oxidant.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS

## RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2003:696722 CAPLUS  
 DOCUMENT NUMBER: 139:219350  
 TITLE: Pharmaceutical dosage forms coated with and acrylic copolymers  
 INVENTOR(S): Peterbeit, Hans-Ulrich; Suefke, Thomas; Meier, Christian; Schnabel, Michael; Blesing, Ingrid; Grimm, Stefan  
 PATENT ASSIGNEE(S): Roehm G.m.b.H. & Co. K.-G., Germany  
 SOURCE: PCT Int. Appl., 49 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO.  | DATE       |
|---|------|----------|------------------|------------|
| WO 2003072087   | A1   | 20030904 | WO 2003-EP934    | 20030130   |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW |      |          |                  |            |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                  |            |
| DE 10208335   | A1   | 20030904 | DE 2002-10208335 | 20020227   |
| CA 2476972  | AA   | 20030904 | CA 2003-2476972  | 20030130   |
| EP 1478352  | A1   | 20041124 | EP 2003-711870   | 20030130   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK   |      |          |                  |            |
| BR 2003008006   | A    | 20050104 | BR 2003-8006     | 20030130   |
| PRIORITY APPLN. INFO.:  |      |          | DE 2002-10208335 | A 20020227 |
|   |      |          | WO 2003-EP934    | W 20030130 |

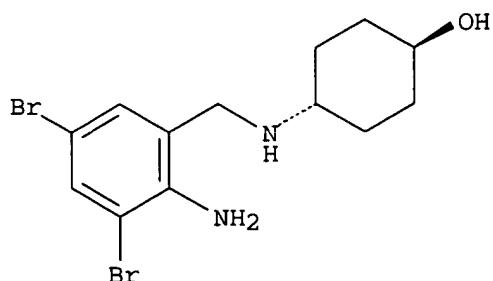
IT 18683-91-5, Ambroxol

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical dosage forms coated with and acrylic copolymers)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB The invention relates to a method for producing a pharmaceutical dosage form as tablets, pellets and/or in the form of an active ingredient-containing matrix, whereby the tablets, pellets and/or active ingredient-containing matrix contain a pharmaceutical active ingredient and a copolymer serving as a coating agent and/or binding agent, and optionally contain a core and pharmaceutically common additives. According to the invention, the copolymer, the pharmaceutical active ingredient, the optionally present core and/or the pharmaceutically common additives are processed using known techniques by melting, injection molding, extrusion, wet granulation, casting, dipping, spreading out, spraying on, or pressing to form tablets, pellets and/or an active ingredient-containing matrix. The inventive method is characterized in that a copolymer is used that consists of 20 to 34 weight % methacrylic acid, 20 to 69 weight % methylacrylate and 0 to 40 weight % ethylacrylate and, optionally, of 0 to 10 weight % of addnl. vinylically copolymerizable monomers with the provision that the glass transition temperature of the copolymer is no higher than 60° according to ISO 11357-2, Item 3.3.3. The invention also relates to the pharmaceutical dosage form produced according to this method, said copolymer and the use thereof. Thus a copolymer was prepared using the monomers: Me acrylate 40; Et acrylate 30; methacrylic acid 30. An emulsion polymerizate containing 30% of the copolymer was mixed with 0.85% sodium lauryl sulfate (in relation to the copolymer); the fluid was dried to a film; the film was soluble in an artificial intestinal juice at pH 6.8.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2002:927238 CAPLUS  
 DOCUMENT NUMBER: 138:323  
 TITLE: Medicament containing an effector of glutathione metabolism together with  $\alpha$ - lipoic acid for use within the framework of artificial kidney therapy  
 INVENTOR(S): Tager, Michael; Ansorge, Siegfried; Fries, Gerhard; Koegst, Dieter  
 PATENT ASSIGNEE(S): Serumwerk Bernburg AG, Germany  
 SOURCE: PCT Int. Appl., 50 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO.  | DATE     |
|---|------|----------|------------------|----------|
| WO 2002096414   | A1   | 20021205 | WO 2002-DE1991   | 20020524 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                  |          |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                  |          |
| DE 10125883   | A1   | 20021212 | DE 2001-10125883 | 20010528 |

|  |    |          |                  |            |
|--|----|----------|------------------|------------|
| EP 1392285   | A1 | 20040303 | EP 2002-747189   | 20020524   |
| EP 1392285   | B1 | 20050209 |                  |            |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,<br>IE, SI, LT, LV, FI, RO, MK, CY, AL, TR |    |          |                  |            |
| BR 2002009732  | A  | 20040914 | BR 2002-9732     | 20020524   |
| JP 2004535410  | T2 | 20041125 | JP 2002-592924   | 20020524   |
| AT 288750  | E  | 20050215 | AT 2002-747189   | 20020524   |
| US 2004127550  | A1 | 20040701 | US 2003-479080   | 20031126   |
| PRIORITY APPLN. INFO.:   |    |          | DE 2001-10125883 | A 20010528 |
|  |    |          | WO 2002-DE1991   | W 20020524 |

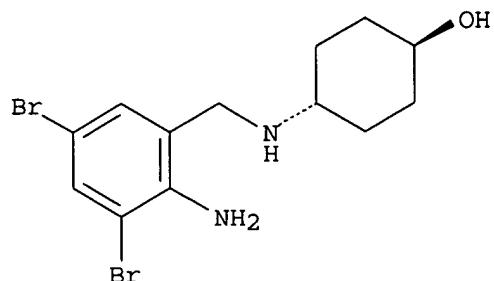
IT 18683-91-5, Ambroxol 18683-91-5D, Ambroxol, prodrug  
derivs.

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(glutathione metabolism effector and  $\alpha$ - lipoic acid  
for use within framework of artificial kidney therapy)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

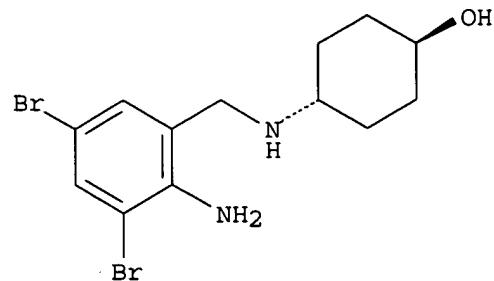
Relative stereochemistry.



RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB The invention relates to a medicament containing an effector of the glutathione metabolism together with  $\alpha$ - lipoic acid, its salts and/or prodrugs, as a combined preparation for the simultaneous, sep. or time-controlled treatment of a defective thiol-disulfide status in artificial kidney therapy in which clin. characteristics indicate a disorder of the thiol-disulfide status of immunocytes. The correction of defective thiol metabolism is of fundamental importance in basic therapy for

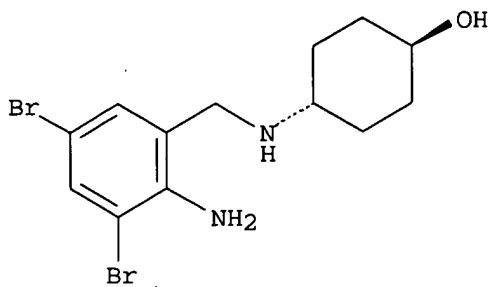
large number of diseases of different origins, in particular, however, in circumstances requiring artificial kidney therapy.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 2002:927223 CAPLUS  
 DOCUMENT NUMBER: 138:330  
 TITLE: Medicament containing an effector of glutathione metabolism and  $\alpha$ - lipoic acid for treating diabetes mellitus  
 INVENTOR(S): Tager, Michael; Ansorge, Siegfried; Fries, Gerhard; Koegst, Dieter  
 PATENT ASSIGNEE(S): Esparma GmbH, Germany; IMTM GmbH  
 SOURCE: PCT Int. Appl., 42 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO.  | DATE       |
|---|------|----------|------------------|------------|
| WO 2002096398   | A2   | 20021205 | WO 2002-EP5811   | 20020527   |
| WO 2002096398   | A3   | 20030227 |                  |            |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                  |            |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  |      |          |                  |            |
| DE 10125882   | A1   | 20021212 | DE 2001-10125882 | 20010528   |
| EP 1392288  | A2   | 20040303 | EP 2002-774028   | 20020527   |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR   |      |          |                  |            |
| JP 2004531567   | T2   | 20041014 | JP 2002-592909   | 20020527   |
| US 2004138311   | A1   | 20040715 | US 2003-478174   | 20031118   |
| PRIORITY APPLN. INFO.:  |      |          | DE 2001-10125882 | A 20010528 |
|   |      |          | WO 2002-EP5811   | W 20020527 |
| IT 18683-91-5, Ambroxol 18683-91-5D, Ambroxol, prodrug derivs.  |      |          |                  |            |
| RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)   |      |          |                  |            |
| (glutathione metabolism effector and $\alpha$ - lipoic acid for treating diabetes mellitus)   |      |          |                  |            |
| RN 18683-91-5 CAPLUS  |      |          |                  |            |
| CN Cyclohexanol, 4-[[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)   |      |          |                  |            |

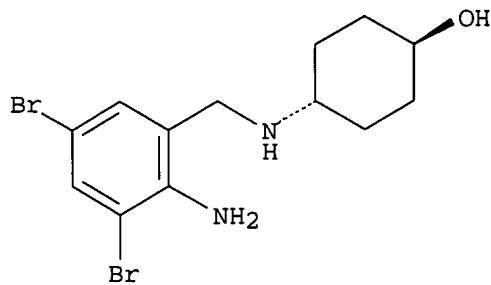
Relative stereochemistry.



RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB The invention provides a medicament containing an effector of glutathione metabolism together with  $\alpha$ - lipoic acid for treating diabetes mellitus. The medicament enables disturbances of thiol-disulfide status or those that occur e.g. in diabetes mellitus to be treated simultaneously, sep., or in a temporally-graduated manner.

L4 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:719652 CAPLUS

DOCUMENT NUMBER: 137:482

TITLE: Protective effect of ambroxol against lung damage in chronically hypoxic rats

AUTHOR(S): Kuang, Tuguang; Zhang, Hongyu; Pang, Baosen; Niu, Shujie; Weng, Xinzhi; Zhang, Jie; Mao, Yanling; Huang, Xiuxia

CORPORATE SOURCE: Beijing Chaoyang Hospital, Beijing Institute of Respiratory Medicine, Beijing, 100020, Peop. Rep. China

SOURCE: Zhongguo Bingli Shengli Zazhi (2001), 17(8), 759-761  
CODEN: ZBSZEB; ISSN: 1000-4718

PUBLISHER: Jinan Daxue

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

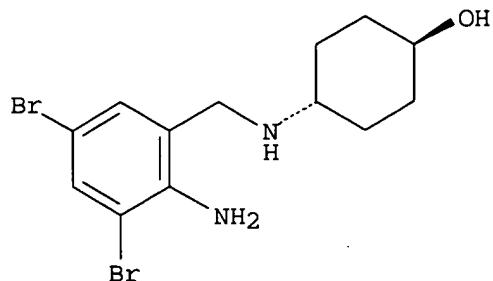
IT 18683-91-5, Ambroxol

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(protective effect of ambroxol against lung damage in chronically hypoxic rats)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB The effect of ambroxol on pulmonary and vascular injury in chronically hypoxic rats was studied. Thirty-six male Wistar rats were randomly divided into 3 groups: normal control, chronically intermittent hypoxia (CIH) and CIH + ambroxol precaution group (AP). The mean pulmonary artery pressure (PAPM) and the levels of superoxide dismutase (SOD) and nitric oxide (NO), **lipid** peroxide in plasma and in the lung homogenate were determined. The SOD and NO levels in plasma and lung homogenate in CIH group were significantly lower than that of normal control and AP group ( $P < 0.01$ ), but the LPO level was significantly higher ( $P < 0.01$ ). PAPM in AP group was significantly lower than that of CIH group ( $P < 0.01$ ); the damage of pulmonary artery smooth muscle cells and extra cell matrix of AP group were much slighter than that of CIH group. Thus, ambroxol might be an effective protector in chronically hypoxic rats.

L4 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:752687 CAPLUS  
 DOCUMENT NUMBER: 133:305464  
 TITLE: Antioxidant activity of mucolytics  
 AUTHOR(S): Strapkova, Anna  
 CORPORATE SOURCE: Ustav farmakologie, Jeseniova Lek. Fakulta, Univ.  
 Komenskeho, Martin, 037 53, Slovakia  
 SOURCE: Farmaceuticky Obzor (2000), 69(8-9), 231-235  
 CODEN: FAOBAS; ISSN: 0014-8172

PUBLISHER: Vydatelstvo Zdravotnickej Literatury HERBA

DOCUMENT TYPE: Journal

LANGUAGE: Slovak

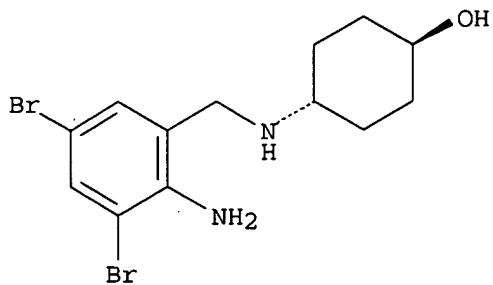
IT 18683-91-5, Ambroxol

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (ambroxol and N-acetylcysteine mucolytic agents effects on trachea and lung smooth muscle reactivity in guinea pigs and relation to antioxidant activity)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB The effects of the mucolytic agents N-acetylcysteine and ambroxol were studied in guinea pigs with respiratory airways reactivity increased by toluene as an agent inducing cell membrane **lipid** peroxidn. The in vitro reactivity of tracheal and lung tissue smooth muscles to histamine was evaluated after animal pretreatment with N-acetylcysteine s.c. or ambroxol i.p. (300 mg/kg) and toluene exposure. The mucolytics were tested also via the inhalation route. No significant changes in the tracheal smooth muscle reactivity were found in the pretreated animals compared to controls. Ambroxol and N-acetylcysteine decreased the lung tissue reactivity. The ambroxol effects were overall stronger than those of N-acetylcysteine. Ambroxol i.p. pretreatment was more effective than the inhalation pretreatment, while N-acetylcysteine was more effective after the inhalation use. The protective effects of mucolytics in the lung tissue may be related to their antioxidant activity, different antioxidant mechanisms, evoked reactivity changes, or other mechanisms.

L4 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:456858 CAPLUS

DOCUMENT NUMBER: 133:94512

TITLE: Improved formulation for topical non-invasive application in vivo

INVENTOR(S): Cevc, Gregor

PATENT ASSIGNEE(S): Idea Innovative Dermale Applikationen G.m.b.H., Germany

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|---|------|----------|-----------------|----------|
| WO 2000038653   | A1   | 20000706 | WO 1998-EP8421  | 19981223 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
| CA 2356080  | AA   | 20000706 | CA 1998-2356080 | 19981223 |
| AU 9925137  | A1   | 20000731 | AU 1999-25137   | 19981223 |
| AU 770803   | B2   | 20040304 |                 |          |
| EP 1140021  | A1   | 20011010 | EP 1998-966846  | 19981223 |

|  |    |          |                   |            |
|--|----|----------|-------------------|------------|
| EP 1140021   | B1 | 20040804 |                   |            |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,<br>IE, SI, LT, LV, FI, RO |    |          |                   |            |
| BR 9816113   | A  | 20011023 | BR 1998-16113     | 19981223   |
| JP 2002533379  | T2 | 20021008 | JP 2000-590607    | 19981223   |
| EE 200100342   | A  | 20021015 | EE 2001-200100342 | 19981223   |
| RU 2207844   | C2 | 20030710 | RU 2001-120008    | 19981223   |
| AT 272391  | E  | 20040815 | AT 1998-966846    | 19981223   |
| HR 2001000309  | A1 | 20020630 | HR 2001-309       | 20010502   |
| NO 2001003164  | A  | 20010822 | NO 2001-3164      | 20010622   |
| US 2002064524  | A1 | 20020530 | US 2001-887493    | 20010622   |
| WO 1998-EP8421   |    |          |                   | A 19981223 |

## PRIORITY APPLN. INFO.:

OTHER SOURCE(S): MARPAT 133:94512

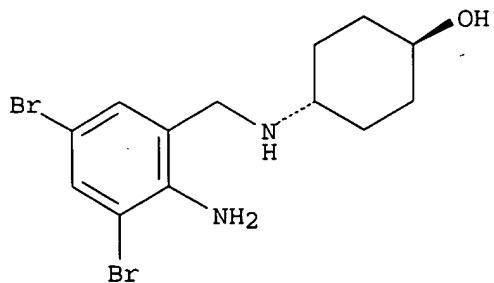
IT 18683-91-5, Ambroxol

RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(penetrating formulation for topical non-invasive application in vivo)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB A formulation comprises mol. arrangements capable of penetrating pores in a barrier, owing to penetrant adaptability, despite the fact that the average diameter of the pores is smaller than the average penetrant diameter, provided that

the penetrants can transport agents or cause permeation through the pores after penetrants have entered pores. The formulation comprises at least 1 consistency builder in an amount that increases the formulation to maximally 5 Nm/s so that spreading over is enabled. The formulation also contains 1 antioxidant in an amount that reduces the increase of oxidation index to <100% per 6 mo and/or at least 1 microbicide in an amount that reduces the bacterial count of 1 million germs added/g of total mass of the formulation to <100 in the case of aerobic bacteria, to <10 in the case of entero-bacteria, and to <1 in the case of Pseudomonas aeruginosa or Staphilococcus aureus, after a period of 4 days. Thus, a composition contained soybean phosphatidylcholine 347, Tween-80 623, sodium dodecyl sulfate 30, benzyl alc. 50, clobetasol 17-propionate 25 and pH 6.5 50 mM phosphate buffer 9000 mg.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:742423 CAPLUS

DOCUMENT NUMBER: 126:27867

TITLE: Effect of paraquat intoxication and ambroxol treatment

on hydrogen peroxide production and **lipid** peroxidation in selected organs of rat

AUTHOR(S) : Piotrowski, Wojciech Jerzy; Pietras, Tadeusz;  
Kurmanowska, Zofia; Nowak, Dariusz; Marczak, Jerzy;  
Marks-Konczalik, Joanna; Mazerant, Piotr

CORPORATE SOURCE: Dep. Pneumol. Allergy, Univ. Lodz, Pol.

SOURCE: Journal of Applied Toxicology (1996), 16(6), 501-507  
CODEN: JJATDK; ISSN: 0260-437X

PUBLISHER: Wiley  
DOCUMENT TYPE: Journal  
LANGUAGE: English

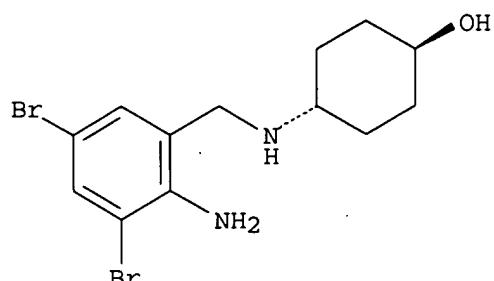
IT 18683-91-5, Ambroxol

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(paraquat intoxication and ambroxol treatment effect on hydrogen peroxide production and **lipid** peroxidn. in selected organs)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB In the present study we examined the concentration of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and various **lipid** peroxidn. products (LPP) such as conjugated dienes (CD), **lipid** hydroperoxides (LH), malonyldialdehyde (MDA) and Schiff bases in selected organs of the rat given a single i.p. dose 35 mg kg<sup>-1</sup> paraquat (Pq). We also evaluated the influence of a mucolytic and probably antioxidant drug, ambroxol, on Pq-induced changes in the concentration of H<sub>2</sub>O<sub>2</sub> and LPP. Paraquat increased the hepatic concentration of H<sub>2</sub>O<sub>2</sub>, CD, LH and MDA by approx. fourfold. Though the dose of Pq was nearly twice the LD<sub>50</sub> dose, we did not notice any changes in the concentration of these substances

in the critical organ, lung or heart and kidney. Ambroxol alleviated the increase of H<sub>2</sub>O<sub>2</sub> in the liver but did not reduce the concentration of LPP. Moreover, the drug administered alone induced **lipid** peroxidn. in the liver. Our results indicate that Pq does not induce H<sub>2</sub>O<sub>2</sub> production and **lipid** peroxidn. in the lung but it increases the concentration of H<sub>2</sub>O<sub>2</sub> and LPP in the liver. Ambroxol inhibits the Pq-induced increase in the concentration of H<sub>2</sub>O<sub>2</sub> in the liver without protecting it against **lipid** peroxidn. Moreover, the drug alone may act as a pro-oxidant.

L4 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

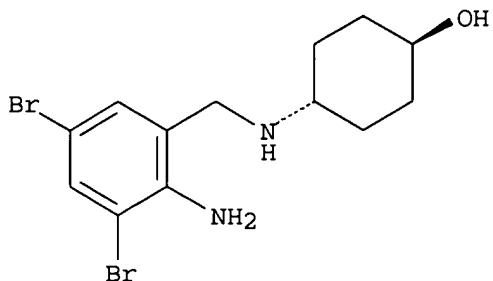
ACCESSION NUMBER: 1995:835170 CAPLUS

DOCUMENT NUMBER: 123:246257

TITLE: Ambroxol inhibits doxorubicin-induced **lipid** peroxidation in heart of mice

AUTHOR(S): Nowak, Dariusz; Pierscinski, Grzegorz; Drzewoski, Jozef  
 CORPORATE SOURCE: Dep. of Pneumonology and Allergology, Medical Univ. of Lodz, Lodz, Pol.  
 SOURCE: Free Radical Biology & Medicine (1995), 19(5), 659-63  
 CODEN: FRBMEH; ISSN: 0891-5849  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 18683-91-5, Ambroxol  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (ambroxol inhibits doxorubicin-induced **lipid** peroxidn. in heart of mice)  
 RN 18683-91-5 CAPLUS  
 CN Cyclohexanol, 4-[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
     (CA INDEX NAME)

Relative stereochemistry.

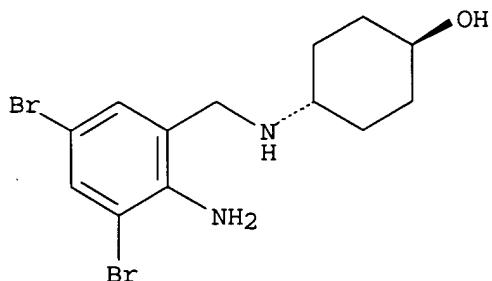


AB A single i.v. injection of doxorubicin (DOX, 30 mg/kg body weight) caused a significant rise in the content of **lipid** peroxidn. products in hearts of mice. The concentration of conjugated dienes (CD) and malondialdehyde (MDA) found 24 h after injection of DOX increased about 1.8- and 2.4-fold and reached values of 11.31 A233/g and 3.72  $\mu$ mol/g, resp. The same dose of 4'-epi-doxorubicin (EPI), a less cardiotoxin epimer of DOX, increased only the heart level of MDA. Both anthracyclines were not able to induce increased formation of CD in murine liver and lungs. Ambroxol, an expectorant drug which possesses the ability to scavenge hydroxyl radicals, injected i.v. (70 mg/kg) 30 min prior to DOX, completely abolished the rise in heart content of CD and MDA. The heart levels of CD and MDA in animals treated with ambroxol and DOX were 3 and 2.7 times lower than those observed in mice treated with water and DOX, resp. Ambroxol had no effect on DOX- and EPI-induced formation of MDA in the lungs. The results indicate that DOX is a more powerful inducer of **lipid** peroxidn. in the heart than EPI and ambroxol may be useful for preventing **lipid** peroxidn. in the heart caused by DOX.

L4 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1995:215096 CAPLUS  
 DOCUMENT NUMBER: 122:742  
 TITLE: Protective effect of ambroxol against heat- and hydrogen peroxide-induced damage to lung **lipids** in mice  
 AUTHOR(S): Nowak, D.; Antczak, A.; Pietras, T.; Bialasiewicz, P. ;

Krol, M.  
 CORPORATE SOURCE: Dept. of Pneumology and Allergology, Medical  
 University of Lodz, Lodz, 90-153, Pol.  
 SOURCE: European Respiratory Journal (1994), 7(9), 1629-34  
 CODEN: ERJOEI; ISSN: 0903-1936  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 18683-91-5, Ambroxol  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antioxidant ambroxol protection against heat- and hydrogen peroxide-induced lung **lipid** peroxidn.)  
 RN 18683-91-5 CAPLUS  
 CN Cyclohexanol, 4-[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.

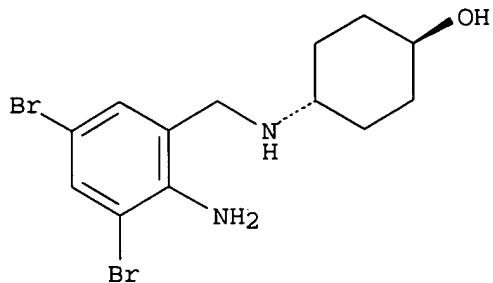


AB We wanted to determine whether ambroxol, a drug which stimulates the release of surfactant by type II pneumocytes, can protect lung **lipids** from peroxidative damage in mice. Animals were injected i.p. with ambroxol, 0.169 mmol·kg<sup>-1</sup>, or 1 mL buffer once a day for three consecutive days. **Lipid** peroxidn. was then induced in lung homogenates either by means of heat, 50°C, or H<sub>2</sub>O<sub>2</sub>, 10 mmol·l<sup>-1</sup>. The lung homogenates from ambroxol-treated animals revealed decreased **lipid** peroxidn. in response to both stimuli. The heat- and H<sub>2</sub>O<sub>2</sub>-induced generation of conjugated dienes (a first **lipid** peroxidn. product) in ambroxol-treated lung homogenates was 3.7 and 3.1 fold lower than in the lungs from buffer-injected mice. Ambroxol, as an inhibitor of heat- and H<sub>2</sub>O<sub>2</sub>-induced **lipid** peroxidn., was equipotent to and stronger than the two antioxidants, N-acetylcysteine and methionine, resp. Ambroxol was not able to protect heart and liver **lipids**. These results suggest that ambroxol can sufficiently enhance the antioxidant defense in lung tissue and can act as a lung **lipid** antioxidant.

L4 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1994:426810 CAPLUS  
 DOCUMENT NUMBER: 121:26810  
 TITLE: Antioxidant properties of Ambroxol  
 AUTHOR(S): Nowak, Dariusz; Antczak, Adam; Krol, Maciej;  
 Bialasiewicz, Piotr; Pietras, Tadeusz  
 CORPORATE SOURCE: Dep. Pneumonology Allergology, Med. Univ. Lodz, Lodz, Pol.  
 SOURCE: Free Radical Biology & Medicine (1994), 16(4), 517-22  
 CODEN: FRBMEH; ISSN: 0891-5849

DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 18683-91-5, Ambroxol  
 RL: BIOL (Biological study)  
 (antioxidant activity of, scavenging of reactive oxygen species in  
 relation to)  
 RN 18683-91-5 CAPLUS  
 CN Cyclohexanol, 4-[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



AB The authors tested whether Ambroxol, a drug which stimulates the release of surfactant by pneumocytes type II, may also possess antioxidant properties. To assess the reactivity of Ambroxol with reactive oxygen species, the authors analyzed its ability to decompose hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and to inhibit the superoxide (O<sub>2</sub>•-) -dependent autoxidn. of pyrogallol, hydroxyl radical (•OH)-mediated deoxyribse oxidation, and hypochlorous acid (HClO)-induced chlorination of monochlorodimedon. Ambroxol was found to be a sufficient scavenger of HClO and •OH and also revealed the capacity to decompose H<sub>2</sub>O<sub>2</sub>. At concns. of 25 and 70 µM, it inhibited HClO-induced chlorination of monochlorodimedon by 22 ± 13 and 59 ± 14%, resp. Similarly, at concns. of 1, 2, and 10 mM, Ambroxol decreased •OH-mediated deoxyribose oxidation by 47 ± 11, 75 ± 9, and 89 ± 4%. In addition, at concns. of 1 to 5 mM, it completely protected linoleic acid from •OH-induced peroxidative damage. Ambroxol had a weak effect on O<sub>2</sub>•--dependent autoxidn. of pyrogallol. The authors' results indicate that Ambroxol has antioxidant activity, which may have clin. significance in protecting lung tissue from oxidant-induced injury.

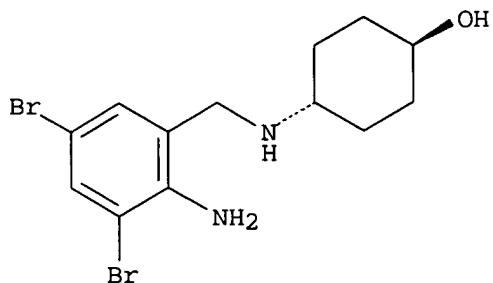
L4 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1994:95731 CAPLUS  
 DOCUMENT NUMBER: 120:95731  
 TITLE: Ambroxol inhibits endotoxin-induced lipid  
 peroxidation in mice  
 AUTHOR(S): Nowak, Dariusz; Pietras, Tadeusz; Antczak, Adam; Krol,  
 Maciej; Piasecka, Grażyna  
 CORPORATE SOURCE: Dep. Pneumonol. Allergol., Med. Acad., Łódź, 90-153,  
 Pol.  
 SOURCE: Polish Journal of Pharmacology (1993), 45(3), 317-22  
 CODEN: PJPAE3; ISSN: 1230-6002  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 18683-91-5, Ambroxol  
 RL: BIOL (Biological study)  
 (lipid peroxidn. induced by endotoxin inhibition by, in heart)

and lung)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB Administration of ambroxol (70 mg/kg i.p.) once a day for 3 days protected lung and heart **lipids** from lipopolysaccharide (LPS, 17 mg/kg) - induced oxidative stress in mice. Ambroxol as a **lipid** peroxidin. inhibitor was almost as active as an equivalent dose of N-acetylcysteine (27.6 mg/kg), a well known antioxidant. The lung and heart levels of conjugated dienes in animals pretreated with ambroxol were 3.3- and 1.7-times lower (and) than those observed in the control group which received only buffer and subsequently LPS. These results indicate that ambroxol can sufficiently inhibit the harmful process of **lipid** peroxidin. in vivo.

L4 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:462779 CAPLUS

DOCUMENT NUMBER: 119:62779

TITLE: The influence of Ambroxol on peroxidative processes in lung and plasma in dogs after pulmonectomy

AUTHOR(S): Jablonka, Stanislaw; Ledwozyw, Andrzej; Kadziolka, Wojciech; Jablonka, Andrzej; Nestorowicz, Andrzej

CORPORATE SOURCE: Dep. Thoracic Cardiac Surg., Medical Acad., Lublin, Pol.

SOURCE: Archivum Veterinarium Polonicum (1992), 32(1-2), 57-66  
CODEN: AVPOEW; ISSN: 0079-3647

DOCUMENT TYPE: Journal

LANGUAGE: English

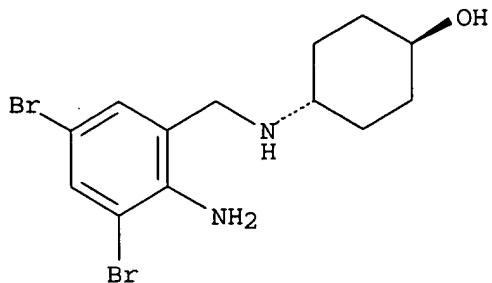
IT 18683-91-5, Ambroxol

RL: BIOL (Biological study)  
(peroxidin. in blood plasma and lung response to)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB The purpose of the studies was to determine the effect of Ambroxol on the activity of antioxidant enzymes and on the glutathione level as well as the intensity of the peroxidative processes in the lung tissue, alveolar macrophages and plasma in dogs after unilateral pulmonectomy. On the 2nd and 6th day after the surgery the activity of antioxidant enzymes and the glutathione level were studied in the remaining lung. The levels of the **lipid peroxidn.** products were determined in the analogous system. In both examined groups the increase in the antioxidant enzyme activity and the **lipid peroxidn.** product levels was observed in the remaining lung after the surgery. In Ambroxol-treated animals the statistically significant increase in the antioxidant enzyme activity was noted while the intensity of peroxidative processes was found to be lower. This fact may suggest that Ambroxol stimulates the resistance of the lung tissue to the free radical activity and inhibits the lung peroxidative processes in dogs after pulmonectomy.

L4 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1993:175674 CAPLUS

DOCUMENT NUMBER: 118:175674

TITLE: Effect of the loading method on the drug release from crosslinked carboxymethyl cellulose beads

AUTHOR(S): Iannuccelli, Valentina; Forni, Flavio; Vandelli, Maria Angela; Bernabei, Maria Teresa

CORPORATE SOURCE: Dep. Pharm. Sci, Univ. Modena, Modena, Italy

SOURCE: Journal of Controlled Release (1993), 23(1), 13-20

CODEN: JCREEC; ISSN: 0168-3659

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 23828-92-4, Ambroxol hydrochloride

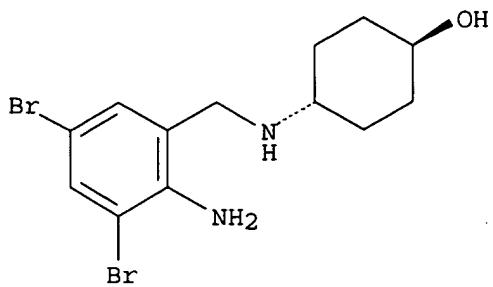
RL: BIOL (Biological study)

(release of, from crosslinked CM-cellulose beads, loading method effect on)

RN 23828-92-4 CAPLUS

CN Cyclohexanol, 4-[[[2-amino-3,5-dibromophenyl)methyl]amino]-, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.

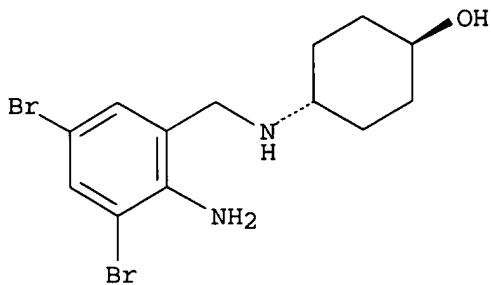


● HCl

AB Spherical matrixes (beads) of crosslinked CM-cellulose were prepared by the **in-lipid** curing coating process using AlCl<sub>3</sub> as curing agent (crosslinker). The loading process was carried out either by adding the drug to the polymer solns. before the extrusion process or be swelling the crosslinked beads in a drug solution. The energy dispersive x-ray anal. showed a homogeneous distribution of both the drug concentration and crosslinking.  
 d. in the network regardless to the loading procedure. When the loading process was carried out before the extrusion process, a residual amount of AlCl<sub>3</sub> remained in the beads. The effects of the residual amount of AlCl<sub>3</sub> on the matrix swelling and drug release processes were analyzed.

L4 ANSWER 17 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1993:160858 CAPLUS  
 DOCUMENT NUMBER: 118:160858  
 TITLE: The effect of ambroxol on peroxidative processes in dog lung mitochondria  
 AUTHOR(S): Ledwozyw, Andrzej; Jablonka, Stanislaw; Tusinska, Elzbieta  
 CORPORATE SOURCE: Zakl. Patofizjol., Akad. Roln., Lublin, Pol.  
 SOURCE: Polskie Archiwum Weterynaryjne (1991), 31(3-4), 105-13  
 CODEN: PARWAC; ISSN: 0079-3647  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Polish  
 IT 18683-91-5, Ambroxol  
 RL: BIOL (Biological study)  
 (lung **lipid** peroxidn. inhibition by, phospholipids in)  
 RN 18683-91-5 CAPLUS  
 CN Cyclohexanol, 4-[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
 (CA INDEX NAME)

Relative stereochemistry.



AB The influence of ambroxol on the Fe<sup>3+</sup>/ADP/dihydroxyfumarate-induced peroxidation of mitochondrial **lipids** in the dog lung was investigated. Changes in mitochondrial **lipid** composition included decreases in phosphatidylcholine and phosphatidylethanolamine content and increases in lysophosphoglyceride content. Addition of ambroxol (5 and 10 mM) to the incubation medium decreased these changes in a concentration-dependent manner. The malondialdehyde production was greatly reduced in the presence of ambroxol. The mode of ambroxol action was comparable to that of other free radical scavengers.

L4 ANSWER 18 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1991:622628 CAPLUS

DOCUMENT NUMBER: 115:222628

TITLE: High-performance liquid chromatography post-column derivatization with fluorescence detection to study the influence of ambroxol on dipalmitoylphosphatidylcholine levels in rabbit eustachian tube washings

AUTHOR(S): Kitsos, M.; Gandini, C.; Massolini, G.; De Lorenzi, E.; Caccialanza, G.

CORPORATE SOURCE: Dep. Pharm. Chem., Pavia, Italy

SOURCE: Journal of Chromatography (1991), 553(1-2), 1-6  
CODEN: JOCRAM; ISSN: 0021-9673

DOCUMENT TYPE: Journal

LANGUAGE: English

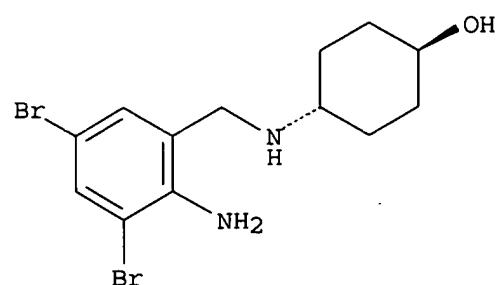
IT 18683-91-5, Ambroxol

RL: BIOL (Biological study)  
(dipalmitoylphosphatidylcholine in eustachian tube washings response to)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB In this work an appropriate HPLC method was set up to guarantee specificity, sensitivity, precision and accuracy in analyzing dipalmitoylphosphatidylcholine (DPPC) in rabbit eustachian tube washings, as well as to determine its varying levels after administration of ambroxol chloride. The procedure is based on a post-column derivatization with fluorescence detection using 1,6-diphenyl-1,3,5-hexatriene which exhibits increased fluorescence in a **lipid** environment. DPPC was chromatographed on a Hypersil C18. The mobile phase for the isocratic elution consisted of 40 mmol/L choline chloride in methanol-tetrahydrofuran (97:3). Ambroxol was given to a group of New Zealand white rabbits at a dose of 30 mg/kg. A second group receiving vehicle only acted as controls.

L4 ANSWER 19 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:509010 CAPLUS

DOCUMENT NUMBER: 111:109010

TITLE: The effects of Oradexon and Ambroxol pretreatment on the oxidative sensitivity of the red blood cells in preterm infants

AUTHOR(S): Novak, Z.; Varga, S. I.; Kovacs, L.; Pal, A.; Pataki, L.; Matkovics, B.

CORPORATE SOURCE: County Munic. Child. Hosp., Szeged, Hung.

SOURCE: Clinica Chimica Acta (1989), 182(3), 241-6

CODEN: CCATAR; ISSN: 0009-8981

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 18683-91-5, Ambroxol

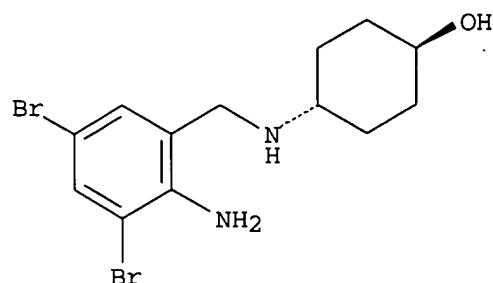
RL: BIOL (Biological study)

(antioxidant enzymes and **lipid** peroxidn. and lung surfactants of newborn response to maternal administration of)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



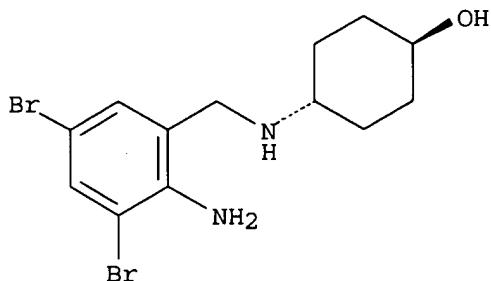
AB The antioxidant enzyme activities and **lipid** peroxidn. in the red blood cells of cord blood were investigated and compared at different gestation times in preterm and full-term neonates, with and without pretreatment of the pregnant mothers with Oradexon (dexamethasone) or Ambroxol. Administration of the 2 drugs not only stimulated the lung surfactant system, but also exerted favorable effects on the antioxidant enzyme activities while the **lipid** peroxidn. was decreased.

L4 ANSWER 20 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1988:137761 CAPLUS

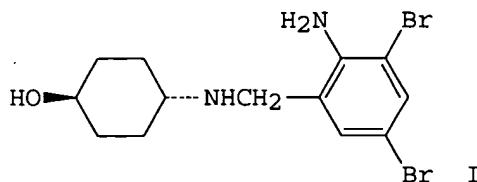
DOCUMENT NUMBER: 108:137761  
 TITLE: Bioavailability of ambroxol sustained release  
 preparations. Part I: in vitro dissolution studies  
 AUTHOR(S): Alighieri, T.; Avanessian, S.; Berlini, S.; Bianchi,  
 S. G.; Deluigi, P.; Valducci, R.; Guelen, P. J. M.  
 CORPORATE SOURCE: Euderma S.r.l., Rimini, Italy  
 SOURCE: Arzneimittel-Forschung (1988), 38(1), 92-4  
 CODEN: ARZNAD; ISSN: 0004-4172  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 IT 23828-92-4, Ambroxol hydrochloride  
 RL: PEP (Physical, engineering or chemical process); PROC (Process)  
 (dissoln. of, from sustained-release capsules based on dialyzing  
 membrane)  
 RN 23828-92-4 CAPLUS  
 CN Cyclohexanol, 4-[(2-amino-3,5-dibromophenyl)methyl]amino]-,  
 monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

GI

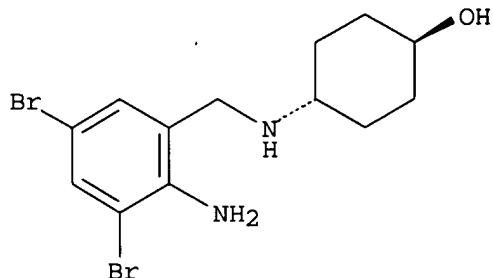


AB The in vitro dissoln. of 2 ambroxol-HCl (I-HCl) sustained-release preps. (75 mg) and the effect of pH of the dissoln. medium on the dissoln. rates were investigated. The studies were carried out using the USP XXI paddle method. A new I-HCl sustained-release formulation based on a dialyzing membrane for controlled release shows a longer release action as compared to a standard sustained release preparation from com. source which is based on spheroids constituted by a lipid matrix. The in vitro release rate of the latter product also appears to be more pH dependent.

L4 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 1987:144014 CAPLUS  
 DOCUMENT NUMBER: 106:144014  
 TITLE: Pharmaceutical granulate with delayed release for oral application  
 INVENTOR(S): Graetzel von Graetz, Jochen; Prochazka, Josef  
 PATENT ASSIGNEE(S): Heumann, Ludwig, und Co. G.m.b.H., Fed. Rep. Ger.  
 SOURCE: Ger. Offen., 8 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

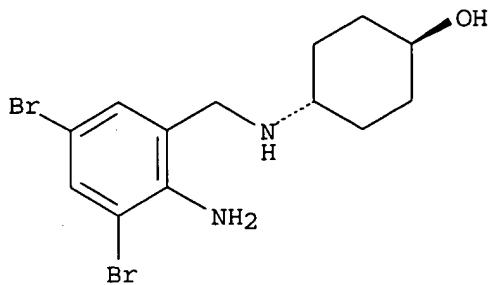
| PATENT NO.  | KIND  | DATE     | APPLICATION NO. | DATE     |
|---|---|----------|-----------------|----------|
| DE 3524003  | A1  | 19870108 | DE 1985-3524003 | 19850704 |
| EP 208144   | A1  | 19870114 | EP 1986-107700  | 19860606 |
| EP 208144   | B1  | 19890920 |                 |          |
| R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE                               |   |          |                 |          |
| AT 46436  | E   | 19891015 | AT 1986-107700  | 19860606 |
| DE 1985-3524003 A 19850704  |   |          |                 |          |
| EP 1986-107700 A 19860606   |   |          |                 |          |
| IT 18683-91-5   | Ambroxol 23828-92-4, Ambroxol hydrochloride |          |                 |          |
| RL: BIOL (Biological study)   | (delayed-release compns. for)               |          |                 |          |
| RN 18683-91-5   | CAPLUS                                      |          |                 |          |
| CN Cyclohexanol, 4-[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI) | (CA INDEX NAME)                             |          |                 |          |

Relative stereochemistry.



RN 23828-92-4 CAPLUS  
 CN Cyclohexanol, 4-[[2-amino-3,5-dibromophenyl)methyl]amino]-, monohydrochloride, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



● HCl

AB A pharmaceutical granulate with delayed release contains a **lipid** of m.p. 40-90° 0.2-10, a gastric juice-insol. powdered film former that is soluble in intestinal juice 0.2-10, an active ingredient soluble in gastric juice and difficultly soluble in intestinal juice 1%, and optionally other formulation adjuvants. Finely powdered ambroxol, HCl 75.0, powdered cellulose acetate phthalate 90.0, and montan wax 70.0 g were mixed and pressed through a perforated disk with 1.0 mm. openings, pulverized, and placed in hard gelatin capsules (235 mg/capsule).

L4 ANSWER 22 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1984:29491 CAPLUS

DOCUMENT NUMBER: 100:29491

TITLE: The perfused rat lung as a model for studies on the formation of surfactant and the effect of ambroxol on this process

AUTHOR(S): Post, M.; Batenburg, J. J.; Schuurmans, E. A. J. M.; Oldenborg, V.; Van der Molen, A. J.; Van Golde, L. M. G.

CORPORATE SOURCE: Lab. Vet. Biochem., State Univ. Utrecht, Utrecht, 3508 TD, Neth.

SOURCE: Lung (1983), 161(6), 349-59

CODEN: LUNGD9; ISSN: 0341-2040

DOCUMENT TYPE: Journal

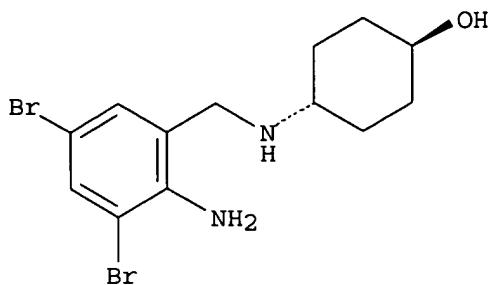
LANGUAGE: English

IT 18683-91-5  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(surfactant phospholipids formation by lung response to)

RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[(2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

Relative stereochemistry.



AB The isolated perfused rat lung was used as a model to investigate the synthesis of surfactant phospholipids from various radioactive precursors and the effect of Ambroxol [18683-91-5], a bronchial secretolytic, on this process. Lungs were ventilated and perfused for periods up to 5 h without detectable development of pulmonary edema. The lungs remained metabolically stable during the entire period of perfusion. Both in whole lung tissue and in the surfactant fraction the radioactive substrates were incorporated predominantly into phosphatidylcholine and phosphatidylglycerol. The degree of saturation of labeled phosphatidylcholines synthesized during perfusion with [methyl-14C]choline, D-[U-14C]glucose, [1(3)-3H]glycerol and [1-14C]palmitate was higher in surfactant than in whole lung tissue. A delayed incorporation into surfactant phospholipids was observed for all precursors. Under the conditions employed, glucose carbon was recovered mainly in the glycerol backbone of phosphatidylcholine and phosphatidylglycerol. Compared to glucose, glycerol appeared to be a minor substrate for lung **lipid** formation. If the lungs were perfused after pretreatment of the rats with Ambroxol on 3 consecutive days, the incorporation of labeled choline and glycerol into pulmonary phospholipids was found to be enhanced. This stimulation was more pronounced in the surfactant fraction than in whole lung tissue. The stimulatory effect on the formation of surfactant **lipids** was smaller after pretreatment of the animals with Ambroxol for 1 day. The results of the present study suggest that Ambroxol may specifically stimulate the synthesis of phospholipids in the alveolar type-II cells and that the drug may not only effect the formation but also the secretion of surfactant **lipids** by these cells.

L4 ANSWER 23 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1983:605920 CAPLUS

DOCUMENT NUMBER: 99:205920

TITLE: Ambroxol and surfactant secretion. Experimental studies on the incorporation of 3H-palmitate into pulmonary surfactant

AUTHOR(S): Kapanci, Yusuf; Elemer, Gabriella

CORPORATE SOURCE: Fac. Med., Univ. Geneva, Geneva, CH-1211, Switz.

SOURCE: Symposia of the Giovanni Lorenzini Foundation (1983), 16 (Pulm. Surfactant Syst.), 263-72

CODEN: SGLFD9; ISSN: 0166-1167

DOCUMENT TYPE: Journal

LANGUAGE: English

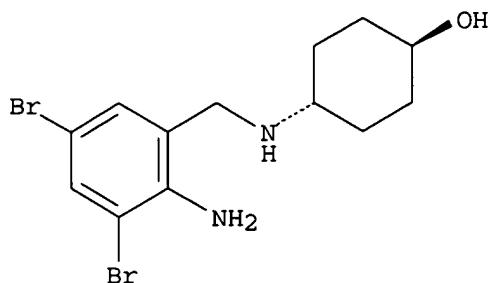
IT 18683-91-5

RL: BIOL (Biological study)  
(lung surfactant formation response to)

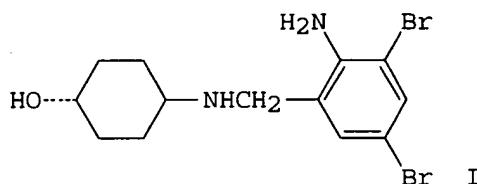
RN 18683-91-5 CAPLUS

CN Cyclohexanol, 4-[[[2-amino-3,5-dibromophenyl)methyl]amino]-, trans- (9CI)  
(CA INDEX NAME)

## Relative stereochemistry.



GI



AB Ambroxol (I) [18683-91-5] was administered to adult rats which were subsequently injected with <sup>3</sup>H-labeled palmitate [57-10-3]. One, 4, and 8 h after injection, the localization of the label in lung tissue was evaluated by electron-microscopic autoradiog., using morphometric methods; its incorporation into **lipids** extracted from lung homogenates and alveolar lavage fluids was also measured. Ambroxol stimulated the rate of incorporation of palmitate into lamellar bodies of type II epithelial cells and into the major surfactant **lipid**, phosphatidylcholine.

L4 ANSWER 24 OF 24 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1977:50790 CAPLUS

DOCUMENT NUMBER: 86:50790

TITLE: NMR studies on the molecular basis of drug-induced phospholipidosis. II. Interaction between several amphiphilic drugs and phospholipids

AUTHOR(S): Seydel, Joachim K.; Wassermann, Otmar

CORPORATE SOURCE: Dep. Pharm. Chem., Borstel Res. Inst., Borstel, Fed. Rep. Ger.

SOURCE: Biochemical Pharmacology (1976), 25(21), 2357-64  
CODEN: BCPCA6; ISSN: 0006-2952

DOCUMENT TYPE: Journal

LANGUAGE: English

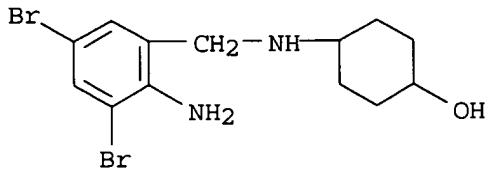
IT 36557-04-7

RL: PRP (Properties)

(interaction of, with phospholipids, phospholipidosis in relation to)

RN 36557-04-7 CAPLUS

CN Cyclohexanol, 4-[(2-amino-3,5-dibromophenyl)methyl]amino]- (9CI) (CA INDEX NAME)



AB The binding of several amphiphilic drugs with phospholipids was studied by NMR; of the drugs studied, most gave a distinct but quant. different interaction with phosphatidylcholine. Increasing lipophilicity of the drugs was correlated with an increase in binding. The degree of signal broadening in the NMR spectra was determined by the ratio of drug/lipid concentration Strong interaction of the drugs occurred with phospholipids,

e.g. phosphatidylcholine and phosphatidylethanolamine, whereas less polar **lipids**, e.g. diacylglycerol or digalactosyldiglyceride, showed no interaction. Cholesterol antagonized the phospholipid/drug interaction. Drug-induced phospholipidosis is apparently caused by interaction of the drug with phospholipids so preventing metabolic degradation of the **lipids**.

| => log Y                                   |            |         |  |
|--|------------|---------|--|
| COST IN U.S. DOLLARS                       | SINCE FILE | TOTAL   |  |
|  | ENTRY      | SESSION |  |
| FULL ESTIMATED COST                        | 125.13     | 286.67  |  |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL   |  |
| CA SUBSCRIBER PRICE                        | ENTRY      | SESSION |  |
|  | -17.52     | -17.52  |  |

STN INTERNATIONAL LOGOFF AT 20:21:31 ON 23 MAR 2005